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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/823,152	04/12/2004	Philip A. Carpino	PC25808A	4558
28523	7590	09/14/2005	EXAMINER	
PFIZER INC. PATENT DEPARTMENT, MS8260-1611 EASTERN POINT ROAD GROTON, CT 06340			OWENS, AMELIA A	
			ART UNIT	PAPER NUMBER
			1625	

DATE MAILED: 09/14/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b> 10/823,152	<b>Applicant(s)</b> CARPINO ET AL.	
	<b>Examiner</b> Amelia A. Owens	<b>Art Unit</b> 1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 30 June 2005.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-4,7-11,30,31,34-36,42,43,49,55 and 59-73 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-4,7-11,30,31,34-36,42,43,49,55 and 59-73 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)  | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

3.0-0

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**DETAILED ACTION**

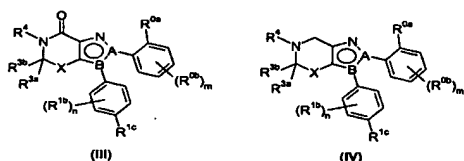
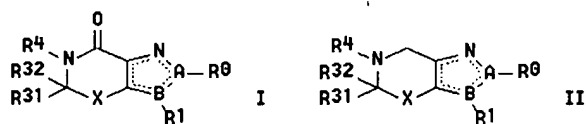
1. Claims 5,6,12-29,32,33,37-41,44-48,50-54,56-58 have been canceled. Claims 1-4,7-11,30,31,34-36,42,43,49,55,59-73 are pending.

**Information Disclosure Statement**

2. The examiner has considered the IDS.

**Election/Restrictions**

3. Applicant's election without traverse of Group I claims 6-11, and claims 1-4,30,31,34-36,42,43,49,55 drawn to compounds below (also included are compounds of formula III and IV) where A is nitrogen, B is carbon and X is a bond in the reply filed on June 30, 2005 is acknowledged.



Applicants' requested rejoinder of method claims according to MPEP 821.04.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

**Claim Rejections - 35 USC § 103**

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

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(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 1,4,30,55 are rejected under 35 U.S.C. 103(a) as being unpatentable over Aebi et al CA 62:299669 @ page 10 of search notes.

Aebi et al teach compounds similar to those claimed. The difference for RN 848-61-3 is the R1 position being Me instead of Et (R1 is CH<sub>2</sub>CH<sub>2</sub>-R1a where R1a is hydrogen). Adjacent homologues without more are presumed to be equivalents. The characteristics normally possessed by members of a homologous series are principally the same, varying gradually from member to member. One of ordinary skill in the art would generally know what to expect in adjacent members. No unexpected or unobvious results are noted.

5. Aebi et al teach compounds similar to those claimed. The difference for RN 887-67-2 is hydrogen instead of phenyl at R4-position. It is noted for RN 848-61-3 the R4-position is phenyl. One of ordinary skill in the art would be motivated to replace the hydrogen with phenyl to arrive at a compound according to the claimed invention given that Aebi teach the interchangeability of hydrogen/phenyl at the R4-position. No unexpected or unobvious results are noted.

6. Claims containing formulas III and IV are not included in the above rejections as the formulas require positions R1/Ro to both be phenyl and the prior art neither teaches nor suggests

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such substitution. Thus, claims 42,43,49,50 contain subject matter neither taught nor suggested by the prior art.

7. Compounds of formula II are not included in the above rejection as the prior art neither teaches nor suggests compounds that the carbon adjacent to the ring nitrogen contains only hydrogen, or as defined by R3a/R3b, all other substituents as defined. See for example, Bosch et al CA 93:168264.

*Claim Rejections - 35 USC § 112*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1-4,7-11,30,31,34-36,42,43,49,55,59-73 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". These factors include 1) the breadth of the claims, 2) the nature of the invention, 3) the state of the prior art, 4) the level of one of ordinary skill, 5) the level of predictability in the art, 6) the amount of direction provided by the inventor, 7) the existence of working examples, and 8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

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**The nature of the invention:** The nature of the invention is the method for treating a disease, condition or disorder modulated by a cannabinoid receptor antagonist comprising administering a compound of claim 1 alone or in combination with an additional pharmaceutical agent; compounds of formula III and IV. See claims 1 and 42 for example.

**The state of the prior art and predictability:** The state of the prior art is that it involves screening in vitro and in vivo to determine which compounds exhibit the desired pharmacological activities (i.e. what compounds can treat which specific disease). There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face. It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. In re Fisher, 427 F. 2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. In the instant case, the instantly claimed invention is highly unpredictable given modulation of a receptor includes inhibition and enhancement.

The exact role of the cannabinoid receptor is still under investigation. Further, there is more than one (1) cannabinoid receptor. See Barth et al 'The development of cannabinoid antagonists' PubMed ID: 10469889 that teach two (2) cannabinoid receptors. Which receptor is applicants' modulating? Moreover, at the time of the invention, there is no umbrella drug known for treatment of all disorders, conditions, diseases related to cannabinoid receptors. One of ordinary skill in the art would have no basis to extrapolate results to compounds structurally removed from those of the prior art.

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Further, applicants' are combining the claimed compound with additional compounds belonging to 'classes' of compounds. See claims 60,61 for example.

**Guidance and working examples:** The tests beginning at page 51 are noted. It is not clear that any of the assays correlate to cannabinoid receptor modulation and any diseases, disorders, condition. There is no evidence of functional treatment, i.e. no correlation to treatment in humans. Applicants have not shown any of the claimed compounds effective via modulation of a cannabinoid receptor for applicants claimed purpose. Applicants' assertions either that the compounds would be effective *or* that the compounds are effective are not enough. Moreover, applicants are claiming ALL diseases, disorders, conditions, known to be associated with modulation of cannabinoid receptors AND such future diseases, disorders, conditions associated with modulation of cannabinoid receptors and such is wholly inoperable.

Thus, the specification fails to provide sufficient support of the broad use of the compounds of claims 1 and 42 for the treatment of any disease. As a result necessitating one of ordinary skill to perform an exhaustive search for which diseases can be treated by which compound of claims 1 and 42 in order to practice the claimed invention.

9. Claims 65,69 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement because claims without any limitation of what is the second ingredient, renders the scope wholly inoperable. The second ingredient can be synergistic, additive, antagonistic, completely blocking the activity of the first ingredient. Therefore, such composition has an operability which cannot be ascertained.

10. Claims 59-73 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims/specification lists nicotine receptor partial agonist,

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opioid antagonist, dopaminergic agent, etc, which can be administered with in combination with the claimed compounds. The listing lacks enablement since the specific dosage change required for the instant compound were not disclosed. In addition, the claims encompass any and all nicotine receptor partial agonist, opioid antagonist, dopaminergic agent, etc, including as yet to be discovered compounds and such is wholly inoperable.

11. Claims 59-73 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Method claims 59-73 encompass as yet unidentified diseases, disorder, conditions associated with the cannabinoid receptor, a description of which is not found in the specification. Further, there are two receptors, (See Barth et al 'The development of cannabinoid antagonists' PubMed ID: 10469889 that teach two (2) cannabinoid receptors). Which receptor is applicants' modulating?

Method claims 59-73 encompass as yet unidentified cannabinoid receptors, a description of which is not found in the specification.

The claims/specification lists nicotine receptor partial agonist, opioid antagonist, dopaminergic agent, etc, which can be administered with in combination with the claimed compounds. Such listing provided no description or guidelines as to 'how' to operate the method employing any and all 'additional pharmaceutical agent'.

The following is a quotation of the second paragraph of 35 U.S.C. 112:



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The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

12. Claims 60,61,65,66,67,70,71 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The terms analog and agent are indefinite. Is it functionally similar? Is it structurally close? The metes and bounds of what would be within the scope of the claims being encompassed by the term 'analog' or 'agent' cannot be ascertained.

***Claim Rejections - 35 USC § 101***

35 U.S.C. 101 reads as follows:


Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

13. Claims 65,69 are rejected under 35 U.S.C. 101 because the claimed invention lacks patentable utility. The claims are drawn to multiple active ingredient composition without naming what the second ingredient is. The second ingredient can have similar activity, opposite activity or completely unrelated activity. Thus, the utility of the combination is unknown and unlimited. Since no guidelines can be given to such unlimited composition, the claims are wholly inoperable in absence of any given nature of the composition.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amelia A. Owens whose telephone number is 571-272-0690. The examiner can normally be reached on Monday - Friday from 8:30 - 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

  
**AMELIA AVERILL OWENS**  
**PRIMARY EXAMINER**